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REVIEW

Embryologically Based Resection of Cervical Cancers: A New Concept of Surgical Radicality

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Abstract *Objectives* With the objective of improving outcomes in oncological surgery, a new concept of surgical anatomy deduced from embryonic development, called ontogenetic anatomy and compartment theory of local tumor spread, is proposed by Michael Höckel from Germany. *Hypothesis* Compartment resection enables the preservation of functionally important tissues of different embryonic origin despite its close proximity to the tumor and incomplete resection of the compartment results in increase in local recurrences. This approach should maximize local tumor control and minimize treatment-related morbidity. *Total Mesometrial Resection (TMMR)* This new surgical technique has been developed and standardized over past 12 years for cervical cancer with a high local control rate without need for adjuvant radiotherapy. *Conclusion* This Embryological based surgery holds a great promise for management of cervical cancer. However this novel surgery needs confirmation in multi institutional settings to translate research into practice for an excellent therapeutic index.

Keywords Compartment theory · Ontogenetic anatomy · Total mesometrial resection · Cervical cancer

Introduction

Till date, the surgical anatomy is established from the study of the mature organism with respect to function. According to traditional principles of cancer surgery, tumor growth is undirected perifocal, irrespective of tissue barriers. During this process, occult and microscopic disease precedes the macroscopic tumor front. Based on this concept, the current standard practice of local cancer surgery has been developed. The established surgical doctrine demands wide tumor excision with metrically defined margins leading to a radical organ resection. This radical surgery is combined with more or less extended lymph node dissection for regional tumor control depending on the type and stage of the malignancy. Despite the correct surgical techniques according to current standards of care with microscopically clear margins (R0 resection), local recurrence rate of solid tumors varies from 5 to 50 % [1]. Hence, adjuvant radiation is recommended for women with histopathological risk factors to reduce locoregional recurrences. However, this is not translated into overall survival. Moreover, there is considerable increase in treatment-related morbidity, due

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to the combined treatment modality [2, 3]. These relatively unfavorable clinical results and inconsistencies in current surgical therapy may challenge the current treatment principles. To overcome this challenge, Höckel proposed a fresh insight at the anatomy based on embryology. He also suggested an alternative concept of local tumor spread, providing the basis for a different definition of local treatment radicality. This novel view of principles of cancer surgery leads to compartment resection, subcompartment resection, supracompartment resection, or multicompartment resection, which has been demonstrated for cervical [4–8] and vulval cancers [9]. Embryologically based surgical anatomy also allows therapeutic lymph node dissection for regional tumor control instead of the standard nodal staging and debulking, rendering adjuvant radiation obsolete. Compartment resection enables the preservation of functionally important tissues of different embryonic origin despite its close proximity to the tumor. The spared autonomic nerves, which are not part of the Müllerian morphogenetic unit, will reduce pelvic organ dysfunction following total mesometrial resection (TMMR), an embryologically based resection for cervical cancer [4–7]. In vulval cancer, the spared tissue is essential for anatomical reconstruction and restoration of structure and function of the vulva [9]. The modern surgery for rectal cancer, called total mesorectal excision, based on developmentally defined topographic anatomy, has already established this principle and has caused a revolution in its treatment results [10, 11]. In this review, an overview of the principles, techniques, and results of embryologically based resection for cervical cancer are discussed.

New Philosophy of Surgical Resection

The study of embryologic and fetal development provides a key to understanding the complex topography of the human pelvis and as a consequence opens up a new insight into the surgical anatomy. This concept is similar to the way we look at the global map, where the geographical boundaries vary depending on what we want to look at. For example, in a political map, the national or state borders are shown, whereas in a physical map, the mountains, deserts, rivers, etc. are depicted which has a completely different outlook.

Höckel et al. [4–7, 9] reconsidered anatomy under the aspect of embryonic development and called it *ontogenetic anatomy*. They proposed the compartment theory of local tumor spread as the basis of surgical therapy for local tumor control. Ontogenetic anatomy attempts to map morphogenetic units in the mature human body in addition to the functional units. Morphogenetic units are differentiated tissue blocks or compartments developed from distinct precursor tissues, the anlage or primordia. An anlage is defined as the earliest discernable tissue complex in the embryo with a fixed morphogenetic determination. Ontogenetic compartments may consist of functional tissues and tissues with no known or apparent physiological function. The compartment theory states that malignant solid tumors are confined to a permissive compartment for a relatively long phase during their natural course, which results from embryonic development as differentiation product of the corresponding anlage. Compartment borders are functionally tumor suppressive. For transgression into adjacent compartments of different embryonic origin, phenotypical changes of the tumor cells are necessary, which evolve relatively late during malignant progression, and even in these late stages a hierarchy of embryological kinship is maintained. Local relapses may arise from remnants of the (stromal) compartment remaining in situ after treatment, harboring or recruiting residual tumor (stem) cells. The compartment theory sets up new principles of surgical radicality for tumor treatment, namely the resection of the tumor-bearing compartment at its borders. Non-lymphatic adjacent tissues of embryologically different compartments can safely be retained, despite their close proximity to the tumor front. Compartment resection should result, on one hand, in maximum local tumor control without adjuvant radiation and, on the other hand, in minimal treatment-related morbidity. Only at the site of intracompartmental resection, a metrically defined tumor-free resection margin has to be achieved.

Cervical Cancer

Current standard principles of cervical cancer surgical therapy are based on the traditional concept of functional anatomy, which is utero-centric and ligament focused. The surgical anatomy of the Wertheim operation ignores the pelvic autonomic nerves. The Wertheim operation is conceptually a wide tumor excision. In a substantial proportion of cases, adjuvant radiotherapy is needed to reduce the development of gross disease in the pelvis as a result of occult or microscopic tumor left behind in the remaining parts of the morphogenetic unit. The traditional five types of the Piver classification of hysterectomy (Class I–V) [12] and the new anatomically based four levels of classification (A, B, C, D, and subtypes) [13] address the wide local excision by tailored parametrectomy. Moreover, extension of the parametrectomy does not improve the local control rate [14]; it only increases the treatment-related morbidity because of unnecessary resection of paracervical tissue containing autonomic nerves and bladder vessels.

Höckel et al. [5] from the Leipzig School of Radical Pelvic Surgery, Germany, proposed a new concept of embryologically based resection of cervical cancer. They

analyzed the development of the genital tract in serial sections of female human embryos and fetuses. They defined the area of resection in adult cadavers, called the distal Müllerian morphogenetic unit. Adding these insights to the previous work on radical hysterectomy with autonomic nerve preservation [15], Michael Höckel invented TMMR for excision of the Müllerian morphogenetic unit for the treatment of cervical cancers.

Ontogenetic Anatomy of the Müllerian Compartment

The development of the genital tract in the human female is important with regard to local spread of carcinoma of the uterine cervix. The formation of female genital organs involves three main developmental processes that produce the ovaries, genital ducts (i.e., fallopian tubes, corpus, cervix uteri, and vagina), and the vulva. The adult genital ducts are derived from the mesodermal paramesonephroid (i.e., Müllerian) ducts, except for the distal vagina, which develops as part of the endodermal urogenital sinus and possibly of the mesonephric (i.e., Wolffian) ducts. The two Müllerian ducts appear in the mesenchyme of the urogenital ridges in male and female human embryos at about 6 weeks of age as an invagination of the coelomic epithelium lateral to the Wolffian ducts. The ducts grow caudally and bend medially beneath the lower pole of the gonads, crossing the Wolffian ducts and ureters. After approaching each other they run further caudally to connect to the urogenital sinus at the sinusal tubercle. Whereas the Müllerian ducts regress during healthy development of the male phenotype, genital duct organogenesis from this cellular aggregation proceeds in the female organs in the seventh week, involving epithelialization, stroma formation, vascularization, and innervation. These processes give rise to three distinct Müllerian morphogenetic subunits in the female adult: proximal, intermediate, and distal. The proximal unit consists of the bilateral fallopian tubes (except the fimbria) and their mesosalpinx. The intermediate unit is the uterine corpus and bilateral peritoneal mesometrium (the so-called broad ligament). Both the proximal and the intermediate Müllerian morphogenetic units are completely covered with peritoneum and are therefore easily identifiable. The three-dimensional view of the subperitoneally located distal Müllerian morphogenetic unit is more complex. Its topography is further complicated due to its attachment to compartments of different embryological origin, such as the genitourinary, rectal, and pelvic parietal compartments. The distal subcompartment consists of the cervix, the proximal two-thirds of the vagina, and their enveloping condensed connective tissue with neurovascular structures, designated as subperitoneal mesometrium. This subperitoneal mesometrium can be discriminated from parametrial and paravaginal tissues of other embryological origin. The uterovaginal (Müllerian) compartment, identified by bottom-up sectional anatomy as the final differentiation product of the Müllerian anlage, is shown schematically in Fig. 1, in the cross-section of fetal pelvis in Fig. 2, and in the adult in Fig. 3. The resection of this compartment is shown at surgical exploration in Fig. 4.

The following structures are integrated into the unit: uterine artery, uterine veins, and uterovaginal branches of the autonomic nerves. During the surgical exposition, understanding of the following terminologies is essential. The subperitoneal mesometrium tapers off with bilateral wings made up of dorsolaterally directed supply tissue with the uterine and vaginal arteries and veins, lymphatic drainage, and a few lymph nodes (referred to as vascular mesometrium) and dorsally directed suspensory and fatty tissue fused to the anterior and lateral mesorectum continuous with the endopelvic fascia overlying the coccygeus muscles (referred to as ligamentous mesometrium). The vascular mesometrium adheres to the bladder and its

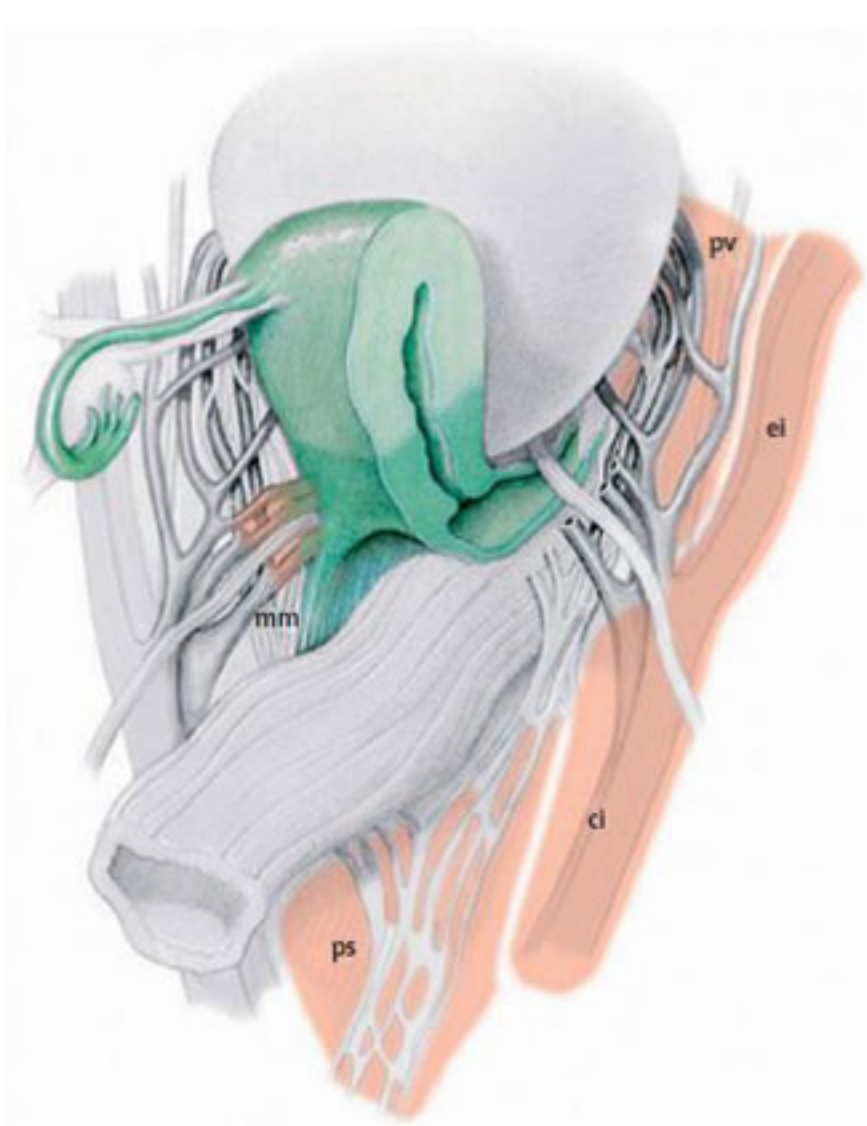

Fig. 1 (Color online) Schematic representation of the Müllerian compartment (*green*) and the pelvic lymph node basins (*orange*) deduced from embryologically based surgical anatomy. *ci* common iliac, *ei* external iliac, *mm* mesometrial, *ps* presacral, *pv* paravisceral. To display the topographic relations, the right half of the compartment and the complete pelvic peritoneal covering are omitted and the visceral branches of the internal iliac vessel system are spread

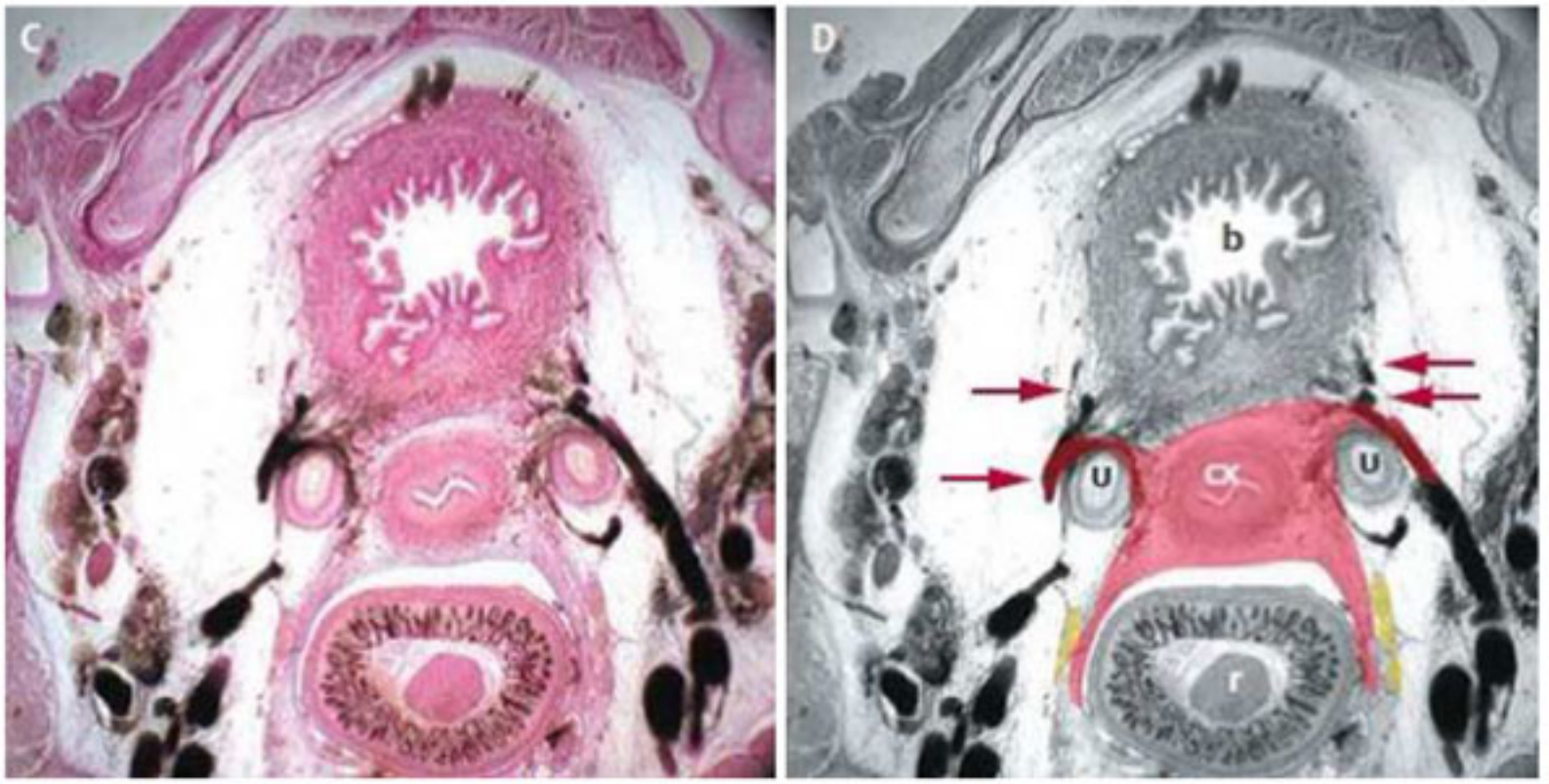

Fig. 2 (Color online) Transverse sections of a female fetus aged 17 weeks at the level where ureters are lateral to cervix. The Müllerian mesenchyme is present as *horseshoe-shaped* condensed connective tissue, with a central core defining the distal Müllerian morphogenetic unit (*red area in D*), pelvic autonomic-nerve plexus (*D, yellow area*). Uterine vessels running anteriorly to ureters (*D, bright red*) are part of the morphogenetic unit (*cx* cervix, *b* bladder, *r* rectum, *red arrows* bladder mesenteries)

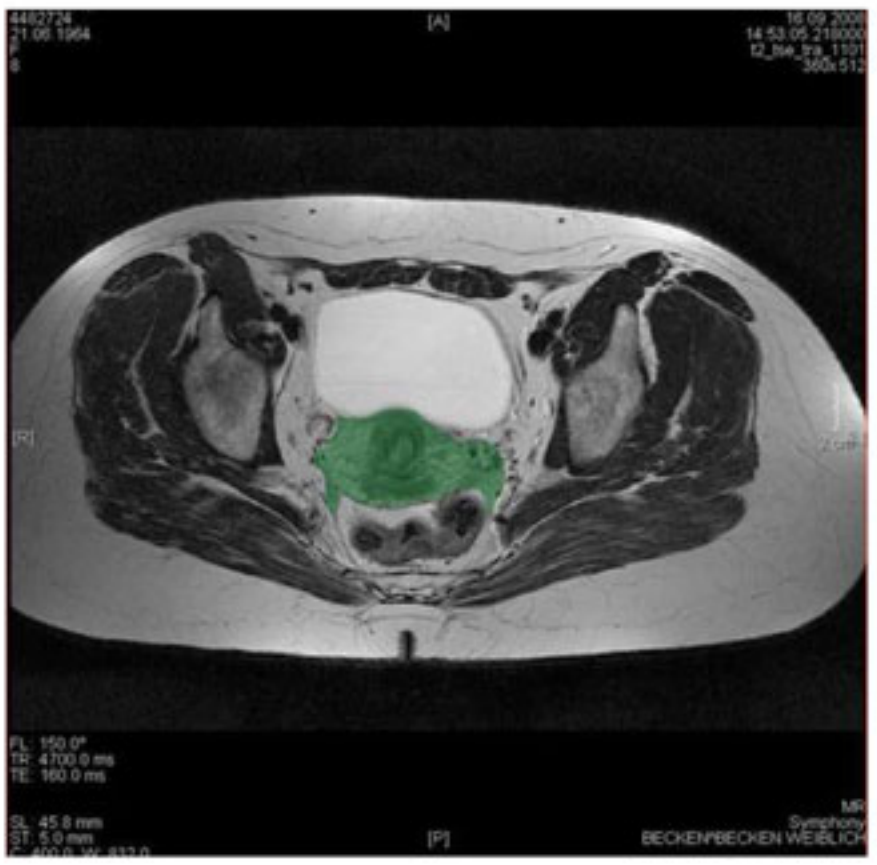

Fig. 3 (Color online) T2-weighted pelvic MRI image of a woman at the level of cervix (*green* Müllerian morphogenetic unit)

mesentery anterolaterally and is traversed by the ureters. The ligamentous mesometrium builds an arc around the anterior mesorectum, to which it is firmly attached, and follows the pelvic curvature sagittally. It is composed of parts of the posterior broad ligaments, uterosacral ligaments, the recto-uterine, rectovaginal ligaments, and the rectovaginal septum. Laterally, the plexus hypogastricus inferior is attached to the ligamentous mesometrium. The subperitoneal part of the Müllerian compartment is a distinct arterial capillary territory covered by continuous lamellae, enabling its complete surgical dissection. However, there are various venous connections to the adjacent bladder and rectum compartments. The pelvic visceroparietal compartments deduced from the embryonic development define the following pelvic parietal lymph node basins (Fig. 1): Lymph nodes in primary basins are external iliac, paravisceral (i.e., anterior internal iliac, suprapobturator and infraobturator, presciatic) and mesometrial. Secondary basin lymph nodes are common iliac (including the superior gluteal) and presacral (i.e., posterior internal iliac, aortic, and caval bifurcation). The different terminologies used for subperitoneal pericervicovaginal tissues in different perspectives are outlined in Table 1.

TMMR: Hypothesis, Principles, Step-by-Step Procedure and Results

Hypothesis

The following are the three hypotheses pertaining to the surgical treatment of cervical cancer:

(1) The resection of the Müllerian compartment and lymph node dissection based on pelvic visceroparietal compartments by TMMR without adjuvant radiation will result in sustained high locoregional tumor control with low morbidity.

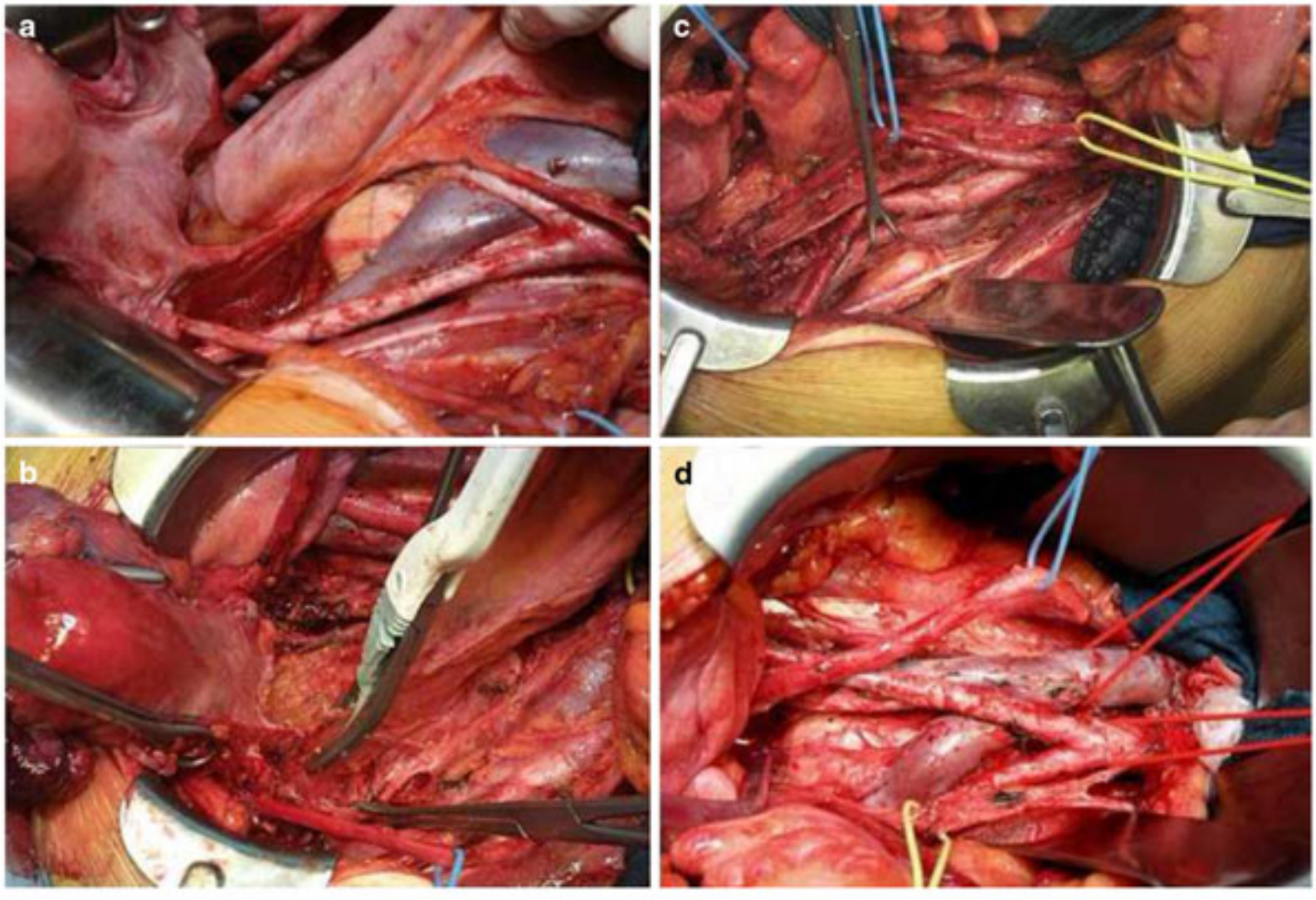

Fig. 4 Resection of this Müllerian compartment with its lymphatic basin at surgical exploration. **a** and **b** posterior dissection of TMMR and **c** and **d** complete lymphadenectomy in pelvic and paraaortic area

Table 1 Terminology of subperitoneal pericervicovaginal tissues

Utero-centric view	Ligament-focused view	Developmental view
Anterior parametrium	Vesicouterine ligament	Proximal bladder mesentery
Lateral parametrium, paracervix, and paracolpium	Cardinal ligament Transverse cervical ligament	Distal bladder mesentery and *vascular mesometrium*
Posterior parametrium	Uterosacral ligament Rectovaginal ligament	*Ligamentous mesometrium* and *mesocolpium*

Note. *Italics* structures integral to the embryologically defined Müllerian compartment

(2) At intact surgically exposable smooth compartment borders, narrow resection margins do not indicate a risk of local tumor recurrence.
(3) Pelvic recurrences after conventional radical hysterectomy arise and propagate at sites of incomplete resection of the Müllerian compartment.

Principles

TMMR is a modified surgery for stage IB–IIB cervical carcinoma. It removes the complete Müllerian compartment except its distal part to preserve a functional vaginal vault. The identification of developmentally deduced pelvic visceroparietal compartments serves as a template for the lymph node basins to be cleared. Extra compartmental non-lymphatic tissues, such as pelvic autonomic nerves and bladder vessels, remain in situ irrespective of their proximity to the malignant tumor if the smooth compartment border is exposable.

Comparison of TMMR and Classical Radical Hysterectomy

TMMR differs from conventional radical hysterectomy by sharp separation of bordering lamellae instead of blunt dissection of the areolar tissues. Although both procedures extirpate the uterus and proximal vagina, the paracervical and paravaginal tissue resected with conventional radical hysterectomy (or radical trachelectomy) is markedly different from that included in the TMMR specimen (Table 2). Conventional techniques tailor the lateral

resection of the paracervix (which, according to the embryological view corresponds to the combined utero-vaginal and bladder mesentery mixed with parietal lymph nodes) to the tumor extension to achieve its wide excision. The tailored posterior subperitoneal resection is not defined with regard to the anterior and anterolateral mesorectal border. Separation from the rectum is often bluntly performed. Non-nerve sparing techniques are still practiced widely disregarding adjacent hypogastric nerves and the inferior hypogastric plexus. Consequently, from the perspective of the Müllerian compartment resection, conventional radical hysterectomy unnecessarily resects paracervical tissue representing autonomic nerves and bladder vessels, thus, increasing treatment-related morbidity. In addition, oncologically important paracervical and paravaginal tissues, which are part of the Müllerian compartment, are retained promoting local recurrences (Fig. 5). Moreover, it can be concluded from the relapse landscape of an unselected group of patients that presacral, gluteal, and presciatic sites might harbor lymph node metastases. These pelvic lymph node basins are routinely cleared with TMMR but not with standard lymph node dissection associated with current radical hysterectomy techniques. The practical differences between TMMR and classical radical hysterectomy are shown in Table 2.

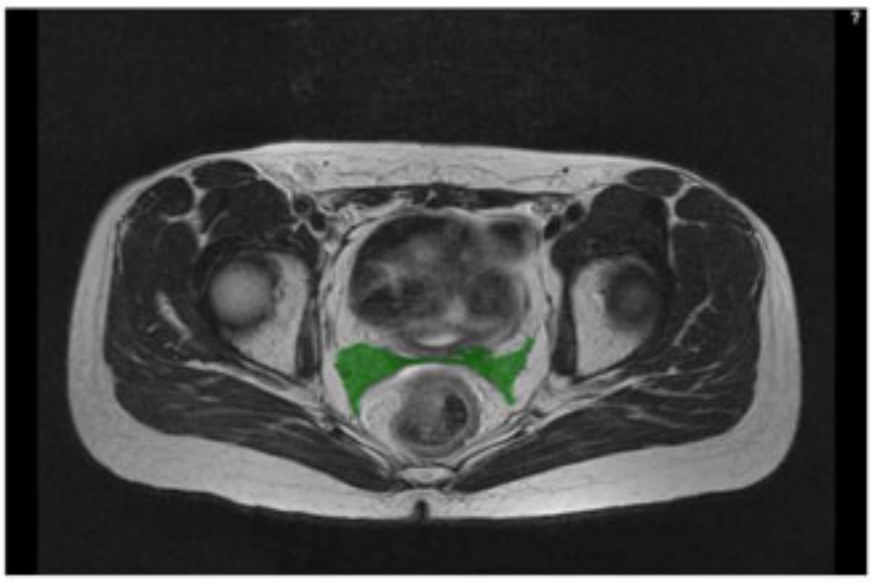

Fig. 5 (Color online) Pelvic MRI demonstrating typical remnants of the Müllerian compartment (*highlighted in green*) after conventional radical hysterectomy (Wertheim operation)

TMMR: Step-by-Step Surgical Procedure

Step 1 Hypogastric midline laparotomy with left circumcision of the umbilicus. In obese patients and for periaortic lymph node dissection, epigastric extension of the incision might be needed.

Step 2 Peritoneal incisions are made to gain access to the pelvic and mid-abdominal retroperitoneum.

Step 3 At the pelvic brim, the infundibulopelvic ligaments and ureters are exposed. The superior hypogastric plexus is identified between the mesosigmoid and the bifurcation of the aorta.

Step 4 The presacral space is developed to the level of S2; the paravisceral spaces are developed to the pubococcygeus and iliococcygeus muscles. The pelvic parietal regions are separated by this maneuvre from the combined urogenital mesenteries. The hypogastric nerves and the upper parts of the inferior hypogastric plexus are exposed too.

Step 5 Complete lymph node dissection is done along the external iliac vessels, internal iliac vessels, and within the obturator fossa.

Table 2 Comparison of TMMR and classical radical hysterectomy

	TMMR	Radical hysterectomy
Oncological principles		
Local control	Compartment resection; wide margins only caudally	Wide tumor excision; radiation for pT2b and close margins
Regional control	Therapeutic lymph node dissection	Nodal staging, eventually debulking; radiation for pN1
Surgical anatomy	Embryologically based	Empirically deduced from the developed organism
Surgical techniques		
Dissection	Sharp	Sharp and blunt
Visceroparietal spaces	Paravisceral and presacral to S2	Paravesical and pararectal
Paracervical resection	Complete mesometrial resection after separation of vascular mesometrium (uterine artery and veins) from bladder mesentery and separation of ligamentous mesometrium (posterior leafs of broad ligaments, uterosacral, rectovaginal ligaments, and rectovaginal septum) from mesorectum and hypogastric nerves, and inferior hypogastric plexuses	Tailored resection of paracervix, uterosacral, and vesicouterine ligaments
Colpotomy	Wide margin	Wide margin

Step 6 Access to the anterior subperitoneal space is gained by sharp separation of the bladder from the cervix and the proximal vagina after incision of the vesicouterine peritoneal fold.

Step 7 The bilateral vascular mesometrium containing the uterine arteries and superficial veins, lymphatics, and a few small lymph nodes is separated completely from the bladder mesentery; the medial aspects of the most distal ureters are exposed.

Step 8 The vascular mesometrium is ligated at the level where uterine vessels branch from the internal iliac vessel system. The deep uterine vein is sealed at its origin and severed.

Step 9 Access to the posterior subperitoneum is obtained by sharp separation of the anterior mesorectum from the proximal vagina and from the ligamentous mesometrium after incision of the rectouterine peritoneal fold and by developing the posterior peritoneal mesometrial wings.

Step 10 After lateral mobilization of the inferior hypogastric plexus, the ligamentous mesometrium corresponding to the uterosacral ligaments in continuity with the uterovaginal support cuff is sealed and transected at the lateral midlevel of the rectum.

Step 11 The vascular mesometrium is dissected en bloc lateromedially and flipped above the ureters.

Step 12 The vesicovaginal venous connections and condensed connective tissue crossing the ureters are ligated and transected over a protecting groove. Subsequently, the distal ureters can be mobilized laterally.

Step 13 After clamping the vagina at a level 2–3 cm distal to the most caudal tumor extension, the anterior vaginal wall is incised. The transverse colpotomy is advanced and completed after sealing the dissection site.

Step 14 Systematic pelvic lymph node dissection is continued by removing the lymph nodes along the common iliac and gluteal vessels. The lumbar branch of the lumbosacral trunk, the proximal sciatic nerve, and the parietal branches of the internal iliac vessels are exposed below the level of the obturator nerve.

Step 15 Presacral lymph node dissection is done caudally to the level of S2. The superior hypogastric plexus and the hypogastric nerves are mobilized and preserved.

Step 16 Systematic periaortic lymph node dissection is done on intra-operative detection of pelvic lymph node metastases. The cranial border of the paracaval, interaortocaval, and paraaortic lymph node dissection is set to the level of the inferior mesenteric artery, if the lymph nodes do not contain metastases. It will be elevated to the left renal vein if periaortic lymph nodes are positive with frozen section analysis.

Step 17 The bladder and rectum peritoneum flaps are sutured together to support the mobilized pelvic ureters.

Step 18 After suprapubic cystostomy and insertion of two capillary draining tubes, the laparotomy is closed. During the operation, lavage of the surgical area is done after every step. Bilateral salpingo-oophorectomy is part of TMMR in postmenopausal women generally if the tumor involves the uterine corpus or on detection of lymph node metastases intraoperatively. The resection yields the characteristic four-winged TMMR specimen covered partly by peritoneum and partly by smooth continuous lamellae (Fig. 6).

Results

Höckel et al. [5] studied serial transverse sections of pelvis of 8 weeks old embryos and of fetuses aged 17–24 weeks. Furthermore, they analyzed the three-dimensional topographic anatomy of fresh (i.e., unfixed) female adult cadavers and other adult cadavers fixed by special Thiel techniques, which maintain the natural color and tissue elasticity [16]. The uterovaginal morphogenetic unit was identified as distinct from the bladder, ureters, rectum, and autonomic nerve plexus in the fetus (Fig. 7). It can also be outlined in whole pelvic cross-sectional specimen and high

Fig. 6 Characteristic four-winged TMMR specimen

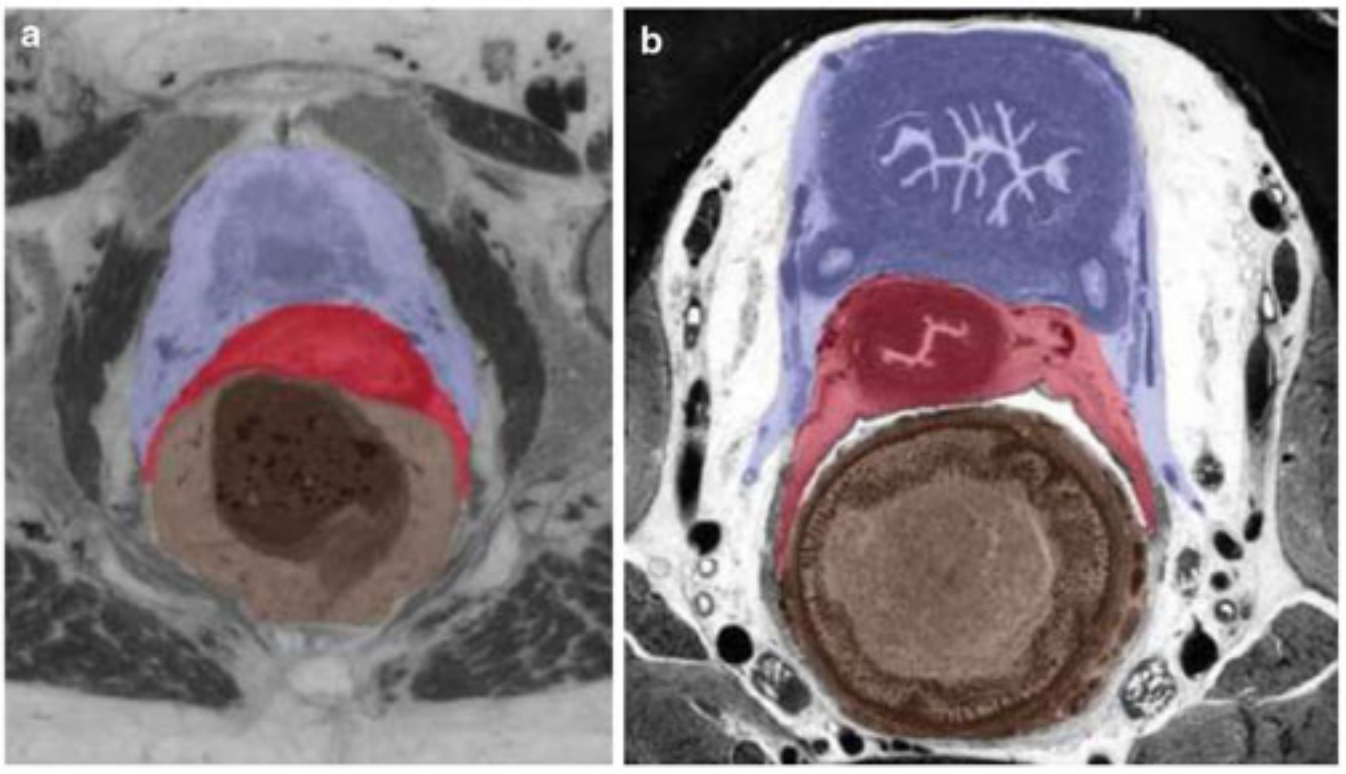

Fig. 7 (Color online) Pelvic visceral compartments in a woman **a** and deduced from development in a 24-week-old female fetus **b**. Images are taken at the level of ureterovesical transition. *Blue* urinary morphogenetic unit, *red* genital morphogenetic unit, *brown* intestinal morphogenetic unit

resolution MRI scans. In situ, the Müllerian compartment can be identified in axial sections of the human female pelvis, such as the Visible Woman Project (National Library of Medicine, NIH, Bethesda ML, USA). In this study, Höckel et al. were unable to derive the presence of either a vesicouterine ligament or a laterally directed cardinal ligament during development of the female genital tract: both structures seem to be artifacts from surgical and cadaver dissection rather than true anatomical structures. They can neither be found in plastinated transverse sections of the human body nor visualized in high-resolution MRI scans. With this background work on embryologically based anatomy, the Müllerian compartment resection, called TMMR, was invented as the new principle for surgical treatment of FIGO stage IB1, IB2, IIA, and selected IIB cervical carcinoma.

A prospective trial at the University of Leipzig, Germany was launched in October 1999 and initial results of 105 cases were published in 2005 [5]. Later in 2007 updated information of 163 cases was reported [6]. The recent results of 212 cases were published in 2009 [7]. Over the past 12 years, the technique of TMMR was standardized. Although over the years some minor modifications in techniques were incorporated, the basic concept of TMMR remains the same. Patients with tumor size 5 cm or more may receive neoadjuvant chemotherapy (5–6 weekly courses of cisplatinum 40 mg/m^2). From 2006 onwards, patients with two and more pelvic lymph node metastases and all patients with periaortic lymph node metastases have been offered adjuvant chemotherapy with up to six courses of cisplatinum 75 mg/m^2 at 3 weeks intervals.

The mean duration of the operative procedure is 6 h. Median time to reach a residual urine volume of 50 mL or less was 9 days. Treatment-related morbidity was low (grade 1 in 35 % and grade 2 in 9 %). On histological examination, 62 % patients with high risk tumors would have been candidates for adjuvant radiation had they been treated with conventional radical hysterectomy. The mean pelvic lymph node count has been 45 + 12. Lymph node metastasis to secondary basins without involvement of primary basins was not observed. Five-year disease-free and overall survival probabilities are 94 and 96 %, respectively, for the whole patient cohort, whereas 5-year disease-free and overall survival probability for the subgroup of patients with stage IB–IIA tumors alone was 98 %. Patients with node-positive disease had a 5-year disease-free and overall survival probability of 81 and 91 %, respectively.

Höckel et al. [7] also generated MRI-based pelvic relapse landscapes from patients who had experienced pelvic failure after conventional radical hysterectomy. The pelvic topography of the peak relapse probability after conventional radical hysterectomy indicates an incomplete resection of the posterior subperitoneal extension of the Müllerian compartment. Figure 5 shows remnants of the Müllerian compartment after classic radical hysterectomy by pelvic MRI.

Another proof of the Müllerian compartment theory in advanced and post-irradiation recurrences is provided in a recent analysis [17]. By pelvic MRI, the authors demonstrated that in locally advanced primary cervical cancers, the major tumor mass was always confined within the uterovaginal compartment, which was inflated or partially destroyed by the neoplasm. About 98 % of stage IIIB tumors were laterally restricted to the Müllerian compartment without evidence of infiltration of the parietal endopelvic fascia. Cases of symmetrical tumor involvement

mirrored the mesenchyme distribution of the Müllerian anlage at the corresponding level within the pelvis. The transgression of these tumors occurring mainly into the bladder may be explained by the embryological kinship between Müllerian system and lower urinary tract. The mesonephric and paramesonephric tissues are both derived from intermediate mesoderm. The mesonephric system participates both in the development of the urinary and genital tract. Tumor fixation at the pelvic wall can no longer be regarded as a general contraindication for surgical treatment as these clinical features may represent fibrotic adherence of the tumor still confined to the uterovaginal compartment with the parietal endopelvic fascia at the levator ani level. Therefore, laterally extended endopelvic resection (LEER), including the en bloc removal of the pelvic floor and side wall muscles to assure the complete multi-compartment extirpation has a high potential of local tumor control in these cases [8, 17–20].

Discussion

As the goal of the operation is literally radical locoregional tumor erasion, adjuvant radiation is completely omitted even in high risk cases. Every step of TMMR is exactly topographically defined. Dissection is precise and anatomically based. TMMR is likely to lead to a low incidence of postoperative anorectal and bladder dysfunction. However, sparing the autonomous nerves in the TMMR operation is not a goal in itself but a logical consequence, because the nerves do not belong to the Müllerian morphogenetic unit. The 5-year overall survival in patients with positive nodes was 91 %, compared with previous reports where similar patients have survival rates of 68–78 % [21, 22]. This can be partly due to routinely clearing the presacral, gluteal, and presciatic lymph nodes in TMMR, which are not part of the standard dissection in radical hysterectomy.

In TMMR it has been shown that close resection margins of even 1 mm or less at the border of the uterovaginal (Müllerian) compartment do not lead to a significant risk of local relapse. However, the pathologist's report of the margin status does not distinguish between a dissection site at the border or within the compartment. The operating time for TMMR is approximately 50 % longer than for conventional radical hysterectomy. This seems to be acceptable because of its benefits. In addition to the improvement in locoregional control, TMMR should result in low treatment-related morbidity not only because the sequelae of adjuvant radiation is avoided but also because inherent to the concept, tissues immediately adjacent to the tumor can be left in situ, if they are of different embryonic origin. Based on historical controls, TMMR without adjuvant radiation has the potential to improve survival by 15–20 %.

The new principle of radicality in surgical oncology in terms of compartment resection can be reduced to subcompartmental and intracompartmental resection for fertility sparing in small and node-negative tumors. It can also be extended to supra- and multi-compartmental resection, including the common root of the urogenital mesentery and eventually the whole internal iliac vessel system. Pelvic multimesovisceral resection and the LEER are further surgical extensions applying the same principle [8, 18–20]. In recent times, it has become a fashion to do everything either laparoscopically or robotically. There are no arguments against doing this operation with either approach.

Till date the experience and results of TMMR are standardized and published by a single center in Germany. Inspired by this work, Trimbos et al. [23] from Leiden University, Netherlands, developed the Swift operation, a modified nerve sparing radical hysterectomy. This surgery is called Swift because the specimen after surgery resembles a swift bird. In this operation, the deep lateral part of the parametrium is not removed, when compared to the traditional radical hysterectomy. To some extent the Swift operation respects the ontogenetic anatomy. The main difference between these two operations is the more extensive lymphadenectomy done in TMMR than in Swift operation.

There is an urgent need for reproducing the results of Höckel et al. in different settings to translate research into practice for an excellent therapeutic index. Hence, wide dissemination of this novel concept to colleagues in different parts of the world is mandatory. The advanced training in the techniques of TMMR after basic surgical training in gynecologic oncology is essential. It may not be possible to completely understand and perform such advanced surgery just by reading the articles and watching online videos. It is possible only by visiting the center in Leipzig, Germany and attending the workshops conducted twice a year with in-depth discussion. One can learn the techniques by witnessing the dissection techniques on cadavers prior to the live surgical demonstration at the center. Updated information can be obtained at http://lsrps.uniklinikum-leipzig.de.

To confirm the results by other centers, a prospective controlled multicenter trial comparing the treatment of patients with cervical cancer stages IB–IIA by TMMR, therapeutic lymph node dissection with or without neoadjuvant chemotherapy, without adjuvant radiation against those receiving standard radical hysterectomy ± adjuvant (chemo) radiation has been set up by the Working Group Gynecologic Oncology (AGO) of the German Society of Obstetrics and Gynecology (Uterus trial # 12).

Conclusion

The developmental view of local tumor spread and surgical anatomy holds a great promise for improving the therapeutic index of the surgical management of cervical cancer and challenges both the classification of radical hysterectomy based on tailored paracervical resection and the indication for adjuvant radiation. Further evaluation with multi-institutional controlled trials is now needed. This novel concept of embryologically based en bloc resection of a malignant solid tumor along the borders of the morphogenetic unit of its origin can be applied to other tumor entities.

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